REMARKS

The Examiner is thanked for the courtesies extended during the course of the interview. Applicants believe that the application is now in condition for allowance, as per the interview discussion and the amendments made herein. Claims 1, 6, 11, 16, 18, 19, 34, 35, 37, 41, 53, 55, 59, 60, 72, and 148 and have been amended. Claims 146, 147 and 154 have been canceled. Support for the amendments can be found throughout the specification and specifically as follows: support for amendment(s) reciting "chemically modified" can be found, *inter alia*, on page 10, lines 17-24.

After the amendments, claims 1-73, 148-149 and 155 are pending in the instant application.

The Office Action was objected to because of undefined use of "SBL" and lack of the verb (s) "is a." Applicants have amended the disclosure to overcome the objections, as agreed during the Interview.

Claims 11-12, 14, 16, 18, 19, 34-35, 48-49, 51, 53, 55, 59-60, 72, 146 and 153 were rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicant regards as the invention. These rejections are respectfully traversed.

Specifically, claims 11, 12, 14, 16, 18, 48, 51, 53 and 55 were, according to the Office Action, indefinite in the recitation of "Protein Data Bank entry" without recitation of the enzyme source. Applicants have amended the claims, where necessary, to recite the source, as was agreed during the interview and suggested in the Office Action. Applicants have also amended the other claims, as was agreed during the interview and suggested in the Office Action, to overcome the remaining indefinite rejections.

Accordingly, reconsideration and withdrawal of the rejections are proper and respectfully requested.

The Office Action rejected claims 1-73, 146-149 and 153-155 under 35 USC 112, first paragraph. These rejections are respectfully traversed.

The Office Action indicated that it was unclear from the specification to what the designation "GG36-WT" referred. During the interview, Examiner and Applicants determined that the specification needed to be amended to recite the wild type to overcome the deficiency, and that the amendment provided no new matter as it was clear "GG36" referred to the wild type (*see, for example, Table 2, Table 30 and Table 31, where "GG36WT", i.e., wild type, is compared to other mutated versions of Subtilisin).* The specification has been amended to indicate that GG36WT is the wild type.

Also, according to the Office Action, Figure 15 "...does not show an improvement of the modified enzyme over the wild-type enzyme..." During the interview, Examiner and Applicants determined that the graph did, in fact, show improvement.

Likewise, according to the Office Action, the significance of assays is lost, because the application does not provide a reference for "suc-AAPF-SBn" (*see* e.g., page 93, line 2-3 of the specification). During the interview, Applicants pointed out the one skilled in the art would know the meaning of the term at the filing date of the application (*see, e.g.*, a copy of *reference* Engineering and Enzyme by Site-directed Mutagenesis to be Resistant to Chemical Oxidation, Estell et al, a copy which is attached herein).

Further, as was discussed during the interview, the unknown quantity in "Table 31" queried in the Office Action refers to margins of error.

As per the amended claims and as determined during the interview, reconsideration and withdrawal of the above-recited rejections are proper and respectfully requested.

The Office Action rejected claims 1-7, 11-28, 37-42, 44, 48-65, 146-148 and 153-155 under 35 USC 112, first paragraph. These rejections are respectfully traversed.

Specifically, according to the Office Action, the disclosure, while "...enabling for subtilisn, does not reasonably provide enablement for the other embodiments..." According to the Office Action, "...another enzyme bound to a targeting moiety may not be active..."

An invention is enabled if one skilled in the art could make and/or use the claimed invention from the disclosure(s) in the patent application without undue experimentation (*see, e.g., MPEP 2164.01 and United States Telectronics, Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed Cir. 1988); *In Re Stephens*, 188 USPQ 659 (CCPA 1976). Whether undue experimentation is needed is based upon the following factors: 1) the quantity of experimentation needed (time and expense); 2) the amount of direction or guidance provided in the specification; 3) the presence or absence of working examples of the invention provided in the specification; 4) the nature of the invention; 5) the state of the prior art; 6) the relative skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims (*see In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

During the interview, it was determined that the rejection in the Office Action was based only upon: 1) the quantity of experimentation needed (time and expense); 3) the presence of absence of working examples (*that there was only a single working*

example of a hydrolase, specifically subtilisin) and 8) the breadth of the claims, and that other factor(s) were not considered (*see* MPEP 2164.01, "It is not necessary that every enablement analysis consider all of the factors.") According to the Office Action, the specification, "...while being enabled for subtilisin, does not provide enablement for the other embodiments of the instant claims." Further, the Office Action asserts, "There has not been any determination or showing that adding cysteines and/or binding the targeting moiety to the enzyme through the *(sic)* a cysteine moiety is operable...Another enzyme bound to a targeting moiety through a cysteine residue may well not have activity."

In the instant case, the claims are drawn to a catalytic antagonist comprising a targeting moiety that is chemically attached to a hydrolase. As discussed during the interview, each embodiment of the present invention has at least two separate parts, a targeting moiety and a hydrolase. The two parts are, as claimed, chemically attached.

The specification need not teach one skilled in the art how to determine whether each embodiment within the scope of the claims is operable, as suggested by the Office Action. Rather, the specification must teach how to make/or use each embodiment within the scope of the claims without undue experimentation. And, since the specification teaches how to make each hydrolase of the embodiment and chemically attach each targeting moiety to the hydrolase (and one skilled in the art using the specification as well as the art available at the filing date of the application could determine, case by case, whether each embodiment was operable), the specification is sufficient under 35 USC 112, first paragraph for each and every embodiment of the claimed invention. Accordingly, as was determined during the interview, reconsideration and withdrawal of the rejections are proper and respectfully requested.

The Office Action rejected claims 1 and 37 under 35 USC 102(b) as being anticipated by Chandragreson. These rejections are traversed. According to the Office Action, the claims read on Chandregason, whether moieties which comprise the chimeric construct come from the same or different sources. However, as was agreed during the interview, the present claims, as amended, are not anticipated or rendered obvious by Chandregason as Chandregason does not disclose or suggest "...a hydrolase and a targeting moiety, which are *chemically* attached..." as recited in the amended claims. Accordingly, reconsideration and withdrawal of the rejections are proper and respectfully requested.

The Office Action rejected claims 1-10, 19-29, 37-47, 56-66, 73, 146-149 and 153-155 under 102(b) over Davis et al. These rejections are traversed. As was agreed during the interview, Davis does not disclose or suggest all the claimed elements (e.g., among other shortcomings, Davis does not disclose or suggest a *targeting moiety* being chemically attached to an hydrolase that degrades the target molecule to reduce binding of the target molecule to its cognate ligand and to said targeting moiety thereby resulting in the release of said antagonist and thereby allowing said antagonist to bind and degrade another targeting molecule); in fact as was agreed, since the Davis reference is directed to glycosylation, it teaches away from the claimed invention, as it does not teach or suggest *targeting*. Accordingly, reconsideration and withdrawal of the rejection are proper and respectfully requested.

The Office Action rejected claims 1, 2, 37 and 38 under 102(b) and claims 1-73, 146-149 and 153-155 under 103(a) over Epenetos et al. These rejections are traversed. According to the Office Action, Epenetos et al teaches a target-cell specific reagent that "...should accumulate at higher avidities to the selected target cells..." However, as

discussed during the interview, Epenetos does not teach or suggest a molecule that can "...degrade...[a] target molecule...thereby resulting...in the release of said antagonist and thereby allowing said antagonist to bind and degrade another targeting molecule." Accordingly, reconsideration and withdrawal of the rejections as applied to claims 1, 2, 37 and 38 are proper and respectfully requested.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance and issuance of a formal Notice of Allowance is respectfully requested. Examiner Patterson is invited to contact Applicants at (650) 846-7544 if there are additional questions/concerns.

Respectfully submitted,

Date: October 17, 2002

H. Thomas Anderton, Jr.
Registration No. 40,895

Genencor International, Inc.
925 Page Mill Road
Palo Alto, CA 94304-1013
Tel: 650-846-7544
Fax: 650-845-6504